

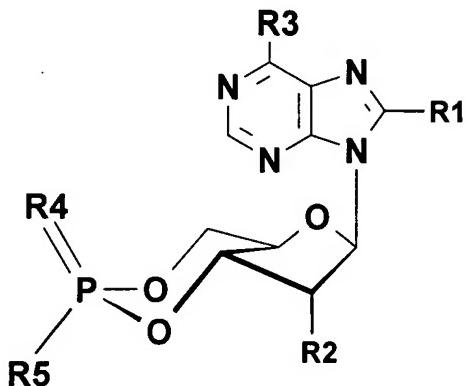
Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claim 1 (original): Compound having the structural formula (I)



and deaza-analogues thereof, wherein:

R₁ can be independently H, halogen, azido, alkyl, aryl, amido-alkyl, amido-aryl, OH, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, SeH, Se-alkyl, Se-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl, cycloalkylamino;

R₂ can be independently H, halogen, azido, O-alkyl, S-alkyl, Se-alkyl, NH-alkyl, N-bisalkyl, alkyl-carbamoyl, cycloalkylamino, silyl;

R₃ can be independently H, halogen, OH, azido, amido-alkyl, amido-aryl, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl, NH-alkyl-carbamoyl, cycloalkylamino;

and wherein

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

R₄ is O(H) or S(H); and

R₅ is O(H), S(H), amino, H, alkyl, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl; or

R₄ is O(H), S(H), amino, H, alkyl, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl; and

R₅ is O(H) or S(H);

and pharmaceutically acceptable salts, esters, and/or solvates thereof,

with the exception of 2'-deoxyadenosine-3',5'-cyclic monophosphate; N⁶-monobutyryl-2'-deoxyadenosine-3',5'-cyclic monophosphate; 2'-deoxyadenosine-3',5'-cyclic monophosphorothioate; 2'-deoxyadenosine-3',5'-cyclic monophosphoroanilidate; 2'-deoxyadenosine-3',5'-cyclic monophosphate methyl triester; 2'-deoxyadenosine-3',5'-cyclic monophosphate ethyl triester; 2'-O-methyladenosine-3',5'-cyclic monophosphate; ; 2'-O-ethyladenosine-3',5'-cyclic monophosphate; 2'-O-n-propyladenosine-3',5'-cyclic monophosphate; 2'-O-n-butyladenosine-3',5'-cyclic monophosphate; 2'-O-iso-butyladenosine-3',5'-cyclic monophosphate; 2'-O-methyladenosine-3',5'-cyclic monophosphate methyl triester; 2'-O-methyladenosine-3',5'-cyclic monophosphate phenyl triester.

Claim 2 (currently amended): ~~Compound as claimed in~~ The compound of claim 1, wherein

R₁ is H, halogen, azido, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, Se-aryl.

Claim 3 (canceled):

Claim 4 (currently amended): The C compound as claimed in of claim 1,2 or 3, wherein

R₁ is H, Br, Cl, I, azido, 2-chlorophenylthio, 3-chlorophenylthio, 4-chlorophenylthio, 2-bromophenylthio, 3-bromophenylthio, 4-bromophenylthio, methylamino, methylthio, ethylthio, n-propylthio, n-butylthio, n-pentylthio, n-hexylthio, 2-fluorophenylthio, 3-fluorophenylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

aminophenylthio, 3-aminophenylthio, 4-aminophenylthio, benzylthio, phenylethylamino, 3-phenyl-propylamino, 2-methoxyphenylthio, 3-methoxyphenylthio, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 2-methylphenylthio, 3-methylphenylthio, 4-methylphenylthio, 2-isopropylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, ethoxy, propoxy, butoxy, benzyloxy, 4-methylbenzyloxy, 4-methoxybenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 4-bromobenzyloxy, phenoxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-aminohexylamino, 2,3-dichlorophenylthio, 2,5-dichlorophenylthio, 2,4-difluorophenylthio, 2,5-dimethoxyphenylthio, 2,5-dimethylthiophenylthio, 2,6-dimethylthiophenylthio, 2,6-dichlorophenylthio.

Claim 5 (currently amended): Compound as claimed in any of the claims 1-4 The compound of claim 1, wherein

R₁ is H, Br, Cl, azido, 2-chlorophenylthio, 3-chlorophenylthio, 4-chlorophenylthio, 2-bromophenylthio, 3-bromophenylthio, 4-bromophenylthio, methylamino, methylthio, ethylthio, n-propylthio, n-butylthio, n-pentylthio, n-hexylthio, 2-fluorophenylthio, 3-fluorophenylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-aminophenylthio, 3-aminophenylthio, 4-aminophenylthio, benzylthio, phenylethylamino, 2-methoxyphenylthio, 3-methoxyphenylthio, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 2-methylphenylthio, 3-methylphenylthio, 4-methylphenylthio, 2-isopropylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, benzyloxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-aminohexylamino, 2,3-dichlorophenylthio, 2,5-dichlorophenylthio, 2,4-difluorophenylthio, 2,5-dimethoxyphenylthio, 2,5-dimethylthiophenylthio, 2,6-dimethylthiophenylthio, 2,6-dimethylthiophenylthio, 2,6-dichlorophenylthio.

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Claim 6 (currently amended): Compound as claimed in any of the claims 1-5 The compound of claim 1, wherein

R₁ is H, Br, Cl, azido, 4-chlorophenylthio, methylamino, methylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-aminophenylthio, benzylthio, n-hexylthio, phenylethylamino, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, ethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 4-methylphenylthio, 3-methoxyphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, benzyloxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-amino hexylamino.

Claim 7 (currently amended): Compound as claimed in any of the claims 1-3 The compound of claim 1, wherein

R₁ is Cl, Br or S-aryl.

Claim 8 (currently amended): Compound as claimed in claim 7 The compound of claim 1, wherein

R₁ is Cl, Br, 4-chlorophenylthio, 4-fluorophenylthio, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 4-methoxyphenylthio, pyridinyl-2-thio, 4-methylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluoro-phenylthio, 4-hydroxyphenylthio, or 2,4-dichloro-phenylthio.

Claim 9 (currently amended): Compound as claimed in claim 7 The compound of claim 7, wherein

R₁ is 4-chlorophenylthio, 4-fluorophenylthio, 4-methoxyphenylthio, 4-methylphenylthio, 4-hydroxyphenylthio.

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Claim 10 (currently amended): ~~Compound as claimed in any of the claims 1-9~~ The compound of claim 1, wherein

R₂ is H, halogen, azido, O-alkyl, S-alkyl.

Claim 11 (currently amended): ~~Compound as claimed in any of the claims 1-10~~ The compound of claim 1, wherein

R₂ is H, Cl, Br, I, O-alkyl, S-methyl, S-ethyl.

Claim 12 (currently amended): ~~Compound as claimed in any of the claims 1-11~~ The compound of claim 1, wherein

R₂ is H, Cl, Br, O-methyl, O-ethyl, O-propyl, O-butyl, O-isobutyl, S-methyl.

Claim 13 (currently amended): ~~Compound as claimed in any of the claims 1-13~~ The compound of claim 1, wherein

R₂ is O-methyl, O-ethyl, O-propyl, O-butyl, O-isobutyl.

Claim 14 (currently amended): ~~Compound as claimed in any of the claims 1-13~~ The compound of claim 1, wherein

R₂ is O-methyl.

Claim 15 (currently amended): ~~Compound as claimed in any of the claims 1-14~~ The compound of claim 1, wherein

R₃ is amino, NH-alkyl, N-bisalkyl, NH-aryl, NH-alkyl-carbamoyl, N-bisalkyl-carbamoyl, amido-alkyl, amido-aryl, OH.

Claim 16 (currently amended): ~~Compound as claimed in any of the claims 1-15~~ The compound of claim 1, wherein

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-phenylcarbamoyl, NH-acetyl, NH-propionyl, NH-butyryl, NH-benzoyl, NH-benzyl, NH-phenylethyl, NH-phenylpropyl, N-bismethyl, N-bisethyl, OH.

Claim 17 (currently amended): ~~Compound as claimed in any of the claims 1-16~~ The compound of claim 1, wherein

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-phenylcarbamoyl; NH-butyryl, NH-benzoyl, NH-benzyl, N-bismethyl, N-bisethyl, OH.

Claim 18 (currently amended): ~~Compound as claimed in any of the claims 1-17~~ The compound of claim 1, wherein

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-benzoyl, N-bismethyl, OH.

Claim 19 (currently amended): ~~Compound as claimed in any of the claims 1-18~~ The compound of claim 1, wherein R_3 is amino, NH-tert-butyl.

Claim 20 (currently amended): ~~Compound as claimed in any of the claims 1-19~~ The compound of claim 1, wherein R_4 and R_5 are independently O(H) or S(H).

Claim 21 (currently amended): ~~Compound as claimed in any of the claims 1-20~~ The compound of claim 1, wherein R_4 and R_5 are O(H).

Claim 22 (currently amended): ~~Compound as claimed in any of the claims 1-21~~ The compound of claim 1, wherein the compound is selected from the group consisting 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-(4-chloro-phenylthio)-N⁶-phenyl-2'-deoxyadenosine-3',5'-cyclic monophosphate;

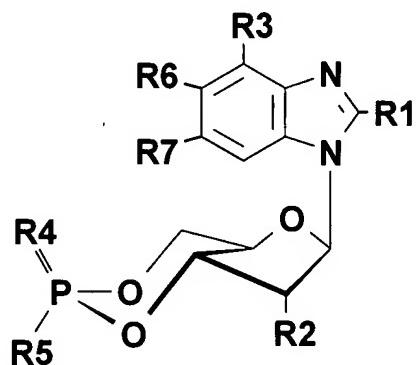
Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

8-bromo-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-methylamino-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-methylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-fluoro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-methyl-cumarinyl-7-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(naphthyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-phenylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-nitro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(2-amino-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-benzylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-n-hexylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-phenylethylamino-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-methoxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-isopropylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(benzimidazolyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(2-hydroxy-ethylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-ethylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2-amino-ethylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(pyridinyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(benzothiazolyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-methyl-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(3-methoxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-isopropyl-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2,3,5,6-tetrafluoro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-hydroxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2,4-dichloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-chloro-phenylthio)-2'-(N,N-dimethyl)-carbamoyl-adenosine-3',5'-cyclic monophosphate;
8-methoxy-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-benzyloxy-2'-O-methyladenosine-3',5'-cyclic monophosphate;

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

8-bromo-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Sp-isomer; 8-bromo-2'-O-methyladenosine-3'-5'-cyclic monophosphorothioate, Rp-isomer, 8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Sp-isomer; 8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Sp-isomer;
8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Sp-isomer; and 8-cyclohexylamino-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-chloro-2'-O-methyladenosine-3',5'-cyclic monophosphate; N⁶-tert-butyl-8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphate; 5,6-Dichloro-1-β-D-ribofuranosyl-2'-O-methylbenzimidazole-3',5'-cyclic monophosphate;

Claim 23 (currently amended): ~~Compound as claimed in any of the claims 1-21~~ The compound of claim 1, wherein the deaza-analogue is a compound having the structural formula II:



wherein

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

R1-R5 are as defined in ~~any of the claims 1-21~~ claim 1, and wherein
R6 and **R7** can be independently H, halogen, alkyl, nitro, amino, and/or alkoxy.

Claim 24 (currently amended): ~~Compound as claimed in~~ The compound of claim 23,
wherein

R1-R3 are as defined in ~~any of the claims 1-21~~;
R4 and **R5** can be independently O or S; and
R6 and **R7** can be independently F, Cl, Br or I.

Claim 25 (currently amended): ~~Compound as claimed in claim 23 or 24~~ The compound
of claim 23, wherein **R6** and **R7** are Cl.

Claim 26 (currently amended): ~~Compound as claimed in claim 23, 24 or 25~~ The
compound of claim 23, wherein R2 is O-alkyl.

Claim 27 (currently amended): ~~Compound as claimed in any of the claims 23-26~~ The
compound of claim 23, wherein

R1 and **R3** are hydrogen;
R2 is O-alkyl; and
R6 and **R7** are Cl.

Claim 28 (currently amended): ~~Compound as claimed in any of the claims 23-27~~ The
compound of claim 23, wherein the deaza-analogue is selected from the group consisting of 1-deaza-adenine analogues, 3-deaza-adenine analogues, 7-deaza-adenine analogues, 1,3-dideaza-adenine analogues, 1,7-dideaza-adenosine analogues and benzimidazole analogues, preferably 5,6-dichlorobenzimidazole.

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

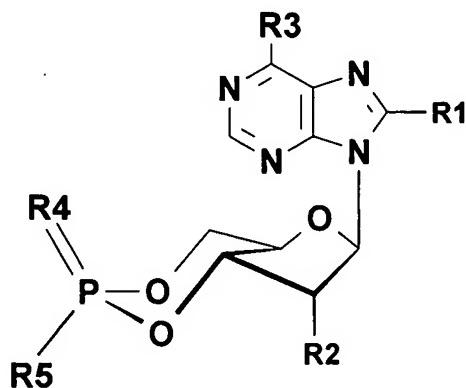
Claim 29 (currently amended): ~~Compound as claimed in any of the claims 1-28~~ The compound of claim 1, wherein said compound modulates for modulating the activity of exchange proteins directly activated by cAMP (Epacs).

Claim 30 (currently amended): ~~Compound as claimed in any of the claims 1-28~~ The compound of claim 1, wherein said compound discriminates for discriminating between Epac- and PKA-mediated signal transduction pathways.

Claim 31 (canceled)

Claim 32 (currently amended): ~~Pharmaceutical A pharmaceutical composition comprising one or more of the compounds as claimed in claims 1-31~~ the compound of claim 1, and one or more pharmaceutically acceptable excipients.

Claim 33 (currently amended): Use of A method for treating a patient comprising administering a pharmaceutical compound comprising a compound having the structural formula (I)



wherein,

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

R_1 can be independently H, halogen, azido, alkyl, aryl, amido-alkyl, amido-aryl, OH, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, SeH, Se-alkyl, Se-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl, cycloalkylamino;

R_2 can be independently H, halogen, azido, O-alkyl, S-alkyl, Se-alkyl, NH-alkyl, N-bisalkyl, alkyl-carbamoyl, cycloalkylamino, silyl;

R_3 can be independently H, halogen, OH, azido, amido-alkyl, amido-aryl, O-alkyl, O-aryl, SH, S-alkyl, S-aryl, amino, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl, NH-alkyl-carbamoyl, cycloalkylamino;

and wherein

R_4 is O(H) or S(H); and

R_5 is O(H), S(H), amino, H, alkyl, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl; or

R_4 is O(H), S(H), amino, H, alkyl, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, N-bisalkyl, N-bisaryl; and

R_5 is O(H) or S(H); and pharmaceutically acceptable salts, esters, and/or solvates thereof
as a medicament.

Claim 34 (canceled)

Claim 35 (currently amended): ~~Use as claimed in~~ The method of claim 33-~~or~~-34, wherein
 R_1 is H, halogen, azido, O-alkyl, O-aryl, S-alkyl, S-aryl, NH-alkyl, NH-aryl, Se-aryl.

Claim 36 (canceled)

Claim 37 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-35, wherein

R_1 is H, Br, Cl, I, azido, 2-chlorophenylthio, 3-chlorophenylthio, 4-chlorophenylthio, 2-bromophenylthio, 3-bromophenylthio, 4-bromophenylthio, methylamino, methylthio, ethylthio,

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

n-propylthio, n-butylthio, n-pentylthio, n-hexylthio, 2-fluorophenylthio, 3-fluorophenylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-aminophenylthio, 3-aminophenylthio, 4-aminophenylthio, benzylthio, phenylethylamino, 3-phenyl-propylamino, 2-methoxyphenylthio, 3-methoxyphenylthio, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 2-methylphenylthio, 3-methylphenylthio, 4-methylphenylthio, 2-isopropylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, ethoxy, propoxy, butoxy, benzyloxy, 4-methylbenzyloxy, 4-methoxybenzyloxy, 4-fluorobenzyloxy, 4-chlorobenzyloxy, 4-bromobenzyloxy, phenoxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-aminohexylamino, 2,3-dichlorophenylthio, 2,5-dichlorophenylthio, 2,4-difluorophenylthio, 2,5-dimethoxyphenylthio, 2,5-dimethylthiophenylthio, 2,6-dimethylthiophenylthio, 2,6-dichlorophenylthio.

Claim 38 (currently amended): Use as claimed in any of the claims of The method of claim 33-37, wherein

R₁ is H, Br, Cl, azido, 2-chlorophenylthio, 3-chlorophenylthio, 4-chlorophenylthio, 2-bromophenylthio, 3-bromophenylthio, 4-bromophenylthio, methylamino, methylthio, ethylthio, n-propylthio, n-butylthio, n-pentylthio, n-hexylthio, 2-fluorophenylthio, 3-fluorophenylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-aminophenylthio, 3-aminophenylthio, 4-aminophenylthio, benzylthio, phenylethylamino, 2-methoxyphenylthio, 3-methoxyphenylthio, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 2-methylphenylthio, 3-methylphenylthio, 4-methylphenylthio, 2-isopropylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, benzyloxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-aminohexylamino, 2,3-dichlorophenylthio,

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

2,5-dichlorophenylthio, 2,4-difluorophenylthio, 2,5-dimethoxyphenylthio, 2,5-dimethylthiophenylthio, 2,6-dimethylthiophenylthio, 2,6-dichlorophenylthio.

Claim 39 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-38, wherein

R₁ is H, Br, Cl, azido, 4-chlorophenylthio, methylamino, methylthio, 4-fluorophenylthio, 4-methylcumarinyl, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 2-aminophenylthio, benzylthio, n-hexylthio, phenylethylamino, 4-methoxyphenylthio, isopropylthio, benzimidazolyl-2-thio, 2-hydroxyethylthio, ethylthio, 2-aminoethylthio, pyridinylthio, benzothiazolylthio, 4-methylphenylthio, 3-methoxyphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluorophenylthio, 4-hydroxyphenylthio, 2,4-dichlorophenylthio, methoxy, benzyloxy, cyclohexylamino, benzylamino, phenylseleno, 4-isopropyloxyphenylthio, 4-methylthiophenylthio, 6-amino hexylamino.

Claim 40 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-39, wherein

R1 is Cl, Br or S-aryl.

Claim 41 (currently amended): ~~Use as claimed in claim 40~~ The method of claim 33, wherein

R1 is Cl, Br, 4-chlorophenylthio, 4-fluorophenylthio, naphtyl-2-thio, phenylthio, 4-nitrophenylthio, 4-methoxyphenylthio, pyridinyl-2-thio, 4-methylphenylthio, 4-isopropylphenylthio, 2,3,5,6-tetrafluoro-phenylthio, 4-hydroxyphenylthio, or 2,4-dichlorophenylthio.

Claim 42 (currently amended): ~~Use as claimed in claim~~ The method of claim 33-40 or 41, wherein

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

R₁ is 4-chlorophenylthio, 4-fluorophenylthio, 4-methoxyphenylthio, 4-methylphenylthio, 4-hydroxyphenylthio.

Claim 43 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-42, wherein

R₂ is H, halogen, azido, O-alkyl, S-alkyl.

Claim 44 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-43, wherein

R₂ is H, Cl, Br, I, O-alkyl, S-methyl, S-ethyl.

Claim 45 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-44, wherein

R₂ is H, Cl, Br, O-methyl, O-ethyl, O-propyl, O-butyl, O-isobutyl, S-methyl.

Claim 46 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-45, wherein

R₂ is O-methyl, O-ethyl, O-propyl, O-butyl, O-isobutyl.

Claim 47 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-45, wherein

R₂ is O-methyl.

Claim 48 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-47, wherein

R₃ is amino, NH-alkyl, N-bisalkyl, NH-aryl, NH-alkyl-carbamoyl, N-bisalkyl-carbamoyl, amido-alkyl, amido-aryl, OH.

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Claim 49 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-48, wherein

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-phenylcarbamoyl, NH-acetyl, NH-propionyl, NH-butyryl, NH-benzoyl, NH-benzyl, NH-phenylethyl, NH-phenylpropyl, N-bismethyl, N-bisethyl, OH.

Claim 50 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-49, wherein

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-phenylcarbamoyl; NH-butyryl, NH-benzoyl, NH-benzyl, N-bismethyl, N-bisethyl, OH.

Claim 51 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-50, wherein

R_3 is amino, NH-phenyl, NH-tert-butyl, NH-tert-butylcarbamoyl, NH-benzoyl, N-bismethyl, OH.

Claim 52 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-51, wherein

R_3 is amino, NH-tert-butyl.

Claim 53 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-51, wherein

R_4 and R_5 are independently O(H) or S(H).

Claim 54 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim 33-51, wherein

R_4 and R_5 are O(H).

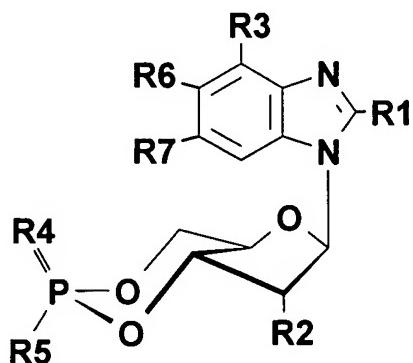
Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Claim 55 (currently amended): . Use as claimed in any of the claims The method of claim 33-54, wherein the compound is selected from the group consisting 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-(4-chloro-phenylthio)-N⁶-phenyl-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-bromo-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-methylamino-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-methylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-fluoro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-methyl-cumarinyl-7-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(naphtyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-phenylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-nitro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2-amino-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-benzylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-n-hexylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-phenylethylamino-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-methoxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-isopropylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(benzimidazolyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2-hydroxy-ethylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-ethylthio-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2-amino-ethylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(pyridinyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(benzothiazolyl-2-thio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-methyl-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(3-methoxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(4-isopropyl-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2,3,5,6-tetrafluoro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

8-(4-hydroxy-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate; 8-(2,4-dichloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-(4-chloro-phenylthio)-2'-(N,N-dimethyl)-carbamoyl-adenosine-3',5'-cyclic monophosphate;
8-methoxy-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-benzyloxy-2'-O-methyladenosine-3',5'-cyclic monophosphate;
8-bromo-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Sp-isomer; 8-bromo-2'-O-methyladenosine-3'-5'-cyclic monophosphorothioate, Rp-isomer, 8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Sp-isomer; 8-(4-chloro-phenylthio)-2'-O-methyladenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-bromo-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Sp-isomer;
8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Rp-isomer; 8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphorothioate, Sp-isomer;
and 8-cyclohexylamino-2'-deoxyadenosine-3',5'-cyclic monophosphate; 8-chloro-2'-O-methyladenosine-3',5'-cyclic monophosphate, N⁶-tert-butyl-8-(4-chloro-phenylthio)-2'-deoxyadenosine-3',5'-cyclic monophosphate.

Claim 56 (currently amended): ~~Use as claimed in any of the claims 21-29; The method of Claim 33,~~ wherein the deaza analogue is a compound having the structural formula II:



Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

wherein

R1-R5 are as defined in ~~any of the claims~~ claim 1-21, and wherein
R6 and **R7** can be independently H, halogen, alkyl, nitro, amino, and/or alkoxy.

Claim 57 (currently amended): ~~Use as claimed in~~ The method of claim 56, wherein
R1-R3 are as defined in ~~any of the claims~~ claim 1-21;
R4 and **R5** can be independently O or S; and
R6 and **R7** can be independently F, Cl, Br or I.

Claim 58 (currently amended): ~~Use as claimed in~~ The method of claim 56-~~or~~-57, wherein
R6 and **R7** are Cl.

Claim 59 (currently amended): ~~Use as claimed in~~ The method of claim 56,~~-57 or 58~~,
wherein **R2** is O-alkyl.

Claim 60 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim
56-~~59~~, wherein

R1 and **R3** are hydrogen;
R2 is O-alkyl; and
R6 and **R7** are Cl.

Claim 61 (currently amended): ~~Use as claimed in any of the claims~~ The method of claim
56-~~60~~, wherein the deaza-analogue is selected from the group consisting of 1-deaza-adenine
analogues, 3-deaza-adenine analogues, 7-deaza-adenine analogues, 1,3-dideaza-adenine
analogues, 1,7-dideaza-adenosine analogues and benzimidazole analogues, preferably 5,6-
dichlorobenzimidazole.

Int'l. Appl. No.: PCT/EP03/06120
Int'l. Filing Date: June 10, 2003
Appl. No.: 10/517,564

Claim 62 (currently amended): ~~Use as claimed in any of the~~ The method of claims 33-61 or 56 ~~in the manufacture of a medicament~~ for the treatment of cancer.

Claim 63 (currently amended): ~~Use as claimed in any of the~~ The method of claims 33-61 or 56 ~~in the manufacture of a medicament~~ for the treatment of chronic inflammation.

Claim 64 (currently amended): ~~Use as claimed in any of the~~ The method of claims 33-61 or 56 ~~in the manufacture of a medicament~~ for the treatment of thrombosis.

Claim 65 (currently amended): ~~Use as claimed in any of the~~ The method of claims 33-61 or 56 ~~in the manufacture of a medicament~~ for the treatment of type-2 diabetes mellitus.

Claim 66 (new): The method of claim 33 wherein said treating is of a human disease.